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Applicant(s): Rabbani et al.

Serial No.: 08/978,637

Filed: November 25, 1997

For: COMPOSITION OF MATTER COMPRISING
PRIMARY NUCLEIC ACID COMPONENT

Group Art Unit: 1635

Examiner: Mary M. Schmidt

527 Madison Avenue, 9th Floor
New York, NY 10022-4304
March 7, 2003

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Commissioner for Patents
Washington, D.C. 20231

**INFORMATION DISCLOSURE STATEMENT
UNDER 37 C.F.R. §§1.56 & 1.97-1.98**

Dear Sirs:

Pursuant to the provisions of 37 C.F.R. §§1.97-1.98, and in full compliance with their duty of disclosure under 37 C.F.R. §1.56, Applicants, through their attorney, are bringing the following eighty-one (81) documents to the attention of the U.S. Patent and Trademark Office and the Examiner handling their above-identified application:

Elazar Rabbani et al.

Serial No. 08/978,637

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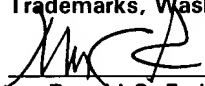
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1. Wu, G.Y. and Wu, C.H., U.S. Patent No. 5,166,320 issued November 24, 1992 [Exhibit 1];
2. Williams, D.A. and Patel, V.P., International Patent Application No. PCT/US95/03817 filed March 27, 1995, published as PCT Patent Application Publication Number WO 95/26200 published October 5, 1995 [Exhibit 2];
3. Ward, D.C. et al., U.S. Patent No. 4,687,732 issued August 18, 1987 [Exhibit 3];
4. Schwartz, D.A. et al., "Construction of a retrotransposon indicator, sequence using a neomycin resistance-encoding gene containing a functional intron," Gene 127:233-236 (1993) [Exhibit 4];
5. Dunn J.J. et al., "Targeting bacteriophage T7 RNA polymerase to the mammalian cell nucleus," Gene 68:259-266 (1988) [Exhibit 5];
6. Fuerst, T.R. et al., et al., "Eukaryotic transient-expression system based on recombinant vaccinia virus that synthesizes bacteriophage T7 RNA polymerase," Proc. Nat Acad. Sci. U.S.A. 83: 8122-8126 (1986) [Exhibit 6];
7. Lieber, A. et al., "High level gene expression in mammalian cells by a nuclear T7-phage RNA polymerase," Nucleic Acids Research 17(21): 8485-8493 (1989) [Exhibit 7];
8. Lieber, A. et al., "[5] Stable High-Level Gene Expression in Mammalian Cells by T7 Phage RNA Polymerase," Methods in Enzymology 217:47-67 (1993)[Exhibit 8];
9. Davenloo, P. et al., "Cloning and expression of the gene for bacteriophage T7 RNA polymerase," Proc. Nat. Acad. Sci. U.S.A. 81: 2035-2039 (1984) [Exhibit 9];
10. Morris, C.E. et al., "Cloning and expression of the bacteriophage T3 RNA polymerase gene," Gene 41:193-200 (1986) [Exhibit 10];

11. Kotani, H. et al., "Nucleotide sequence and expression of the cloned gene of bacteriophage SP6 RNA polymerase," Nucleic Acids Research 15(6):2653-2664 (1987) [Exhibit 11];
12. Dubendorff, J.W. and Studier, F.W., "Creation of a T7 Autogene – Cloning and Expression of the Gene for Bacteriophage T7 RNA Polymerase under Control of Its Cognate Promoter," Journal of Molecular Biology 219: 61-68 (1991) [Exhibit 12];
13. Dahlberg, J.E. and Lund, E., "The Genes and Transcription of the Major Small Nuclear RNAs," in Structure and Function of Major and Minor Small Nuclear Ribonucleoprotein Particles, Birnstiel, M. Ed., Springer Verlag, Berlin, Heidelberg, NY, London, Paris, Tokyo , pp. 38- 70 (1988)) [Exhibit 13];
14. Zieve, G.W. and Sautereau, R.A., "Cell Biology of the snRNP Particles," Biochemistry and Molecular Biology 25(1):1-46 (1990) [Exhibit 14];
15. Izant, J.G. and Sardelli, A.D., "Antisense Inhibitor of RNA Splicing," in Current Communications in Molecular Biology, Antisense RNA and DNA, Melton, D.A., Ed., Cold Spring Harbor Laboratory, pp. 141-149 (1988) [Exhibit 15]
16. You, C-Y and Weiner, A.M., "A U1 Small Nuclear Ribonucleoprotein Particle with Altered Specificity Induces Alternative Splicing of an Adenovirus E1A mRNA Precursor," Molecular and Cellular Biology 9(8):3429-3437 (1989)) [Exhibit 16]
17. Chen, C.J. et al., "Inhibition of HIV-1 Replication by Novel Multitarget Ribozymes," Antisense Strategies, Annals of the New York Academy of Sciences 660:271-273 (1992) [Exhibit 17]
18. Zhou Z. et al., "Inhibition of HIV-1 in human T-lymphocytes by retrovirally transduced anti-*tat* and *rev* hammerhead ribozymes," Gene 149:33-39 (1994) [Exhibit 18]
19. Lisiewicz, J. et al., "Inhibition of human immunodeficiency virus type 1 replication by regulated expression of a polymeric Tat activation response RNA decoy as a strategy for gene therapy in AIDS," Proc. Natl. Acad. Sci. USA 90:8000-8004 (1993) [Exhibit 19]

20. Husson, R.N. et al., "Phase I study of continuous-infusion soluble CD4 as a single agent and in combination with oral dideoxyinosine therapy in children with symptomatic human immunodeficiency virus infection," The Journal of Pediatrics 121(4):621-633 (1992) [Exhibit 20]
21. Yu, M. et al., "Progress towards gene therapy for HIV infection," Gene Therapy 1:13-16 (1994) [Exhibit 21]
22. Sczakiel, G. et al., "Tat- and Rev-Directed Antisense RNA Expression Inhibits and Abolishes Replication of Human Immunodeficiency Virus Type 1: a Temporal Analysis," Journal of Virology 66(9):5576-5581 (1992) [Exhibit 22]
23. Sczakiel, G. and Pawlita, M., "Inhibition of Human Immunodeficiency Virus Type 1 Replication in Human T Cells Stably Expressing Antisense RNA," Journal of Virology 65(1):468-472 (1991) [Exhibit 23]
24. Cotton, M. and Birnstiel, M.L., "Ribozyme mediated destruction of RNA *in vivo*," The EMBO Journal 8(12):3861-3866 (1989) [Exhibit 24]
25. Nichols, R. et al., "A universal nucleoside for use at ambiguous sites in DNA primers," Nature 369:492-493 (1994)] [Exhibit 25]
26. Eritja, R. et al., "Synthesis and properties of oligonucleotides containing 2'-deoxynebularine and 2'-deoxyxanthosine," Nucleic Acids Research 14(20):8135-8153 (1986) [Exhibit 26]
27. Engelhardt D., et al., U.S. Patent No.5, 260,433 issued November 9, 1993 [Exhibit 27]
28. Ward D.C. et al., U.S. Patent No. 4,711,955 issued December 8, 1987 [Exhibit 28]
29. Engelhardt D. et al., U.S. Patent No. 5,241,060 issued August 31, 1993 [Exhibit 29]
30. Stavrianouloulos, J., U.S. Patent No. 4,707,440 issued November 17, 1987 [Exhibit 30]

31. Lever, A.M.L., "Gene Therapy for HIV Infection," British Medical Bulletin 51(1):149-166 (1995) [Exhibit 31]
32. Wu, C.H. et al., "Targeting Genes: Delivery and Persistent Expression of a Foreign Gene Driven by Mammalian Regulatory Elements *in Vivo*," The Journal of Biological Chemistry 264(29):16985-16987 (1989) [Exhibit 32]
33. Wagner, E. et al., "Coupling of adenovirus to transferring-polylysine/DNA complexes greatly enhances receptor-mediated gene delivery and expression of transfected genes," Proc. Natl. Acad. Sci. USA 89:6099-6103 (1992) [Exhibit 33]
34. Ruoslahti, E. et al., "Alignment of Biologically Active Domains in the Fibronectin Molecule," The Journal of Biological Chemistry 256(14):7277-7281 (1981) [Exhibit 34]
35. Cristiano, R.J. et al., "Hepatic gene therapy: Adenovirus enhancement of receptor-mediated gene delivery and expression in primary hepatocytes," Proc. Natl. Acad. Sci. USA 90:2122-2126 (1993) [Exhibit 35]
36. Curiel, D.T. et al., "Adenovirus enhancement of transferring-polylysine-mediated gene delivery," Proc. Natl. Acad. Sci. USA 88:8850-8854 (1991) [Exhibit 36]
37. Wagner, E. et al., "Influenza virus hemagglutinin HA-2 N-terminal fusogenic peptides augment gene transfer by transferring-polylysine-DNA complexes: Toward a synthetic virus-like gene-transfer vehicle," Proc. Natl. Acad. Sci. USA 89:7934-7938 (1992) [Exhibit 37]
38. Argos, P. et al., "The integrase family of site-specific recombinases: regional similarities and global diversity," The EMBO Journal 5(2):433-440 (1986) [Exhibit 38]
39. Brakel et al., [U.S. Patent Application Serial No. 07/446,235 [Exhibit 39]*

40. Kessler, C., "Detection of Nucleic Acids by Enzyme-Linked Immuno-Sorbent Assay (ELISA) Technique: An Example for the Development of a Novel Nonradioactive Labeling and Detection System With High Sensitivity," in Advances in Mutagenesis Research 1, Obe, G. Ed., Springer Verlag, Berlin, 105-152 (1990) [Exhibit 40]
41. Rigby, P.W. et al., "Labeling Deoxyribonucleic Acid to High Specific Activity in Vitro by Nick Translation with DNA Polymerase," Journal of Molecular Biology 113:237-251 (1977) [Exhibit 41]
42. Saiki, R. et al., "Primer-Directed Enzymatic Amplification of DNA with a Thermostable DNA Polymerase," Science 239:487-491 (1985) [Exhibit 42]
43. Melton, D.A. et al., "Efficient in vitro synthesis of biologically active RNA and RNA hybridization probes from plasmids containing a bacteriophage SP6 promoter," Nucleic Acids Research 12(18):7035-7056 (1984) [Exhibit 43]
44. Roychoudhury, R. et al., "Influence of nucleotide sequence adjacent to duplex DNA termini on 3' terminal labeling by terminal transferase," Nucleic Acids Research 6(4):1323-1333 (1979) [Exhibit 44]
45. Cook, A.F. et al., "Synthesis and hybridization of a series of biotinylated oligonucleotides," Nucleic Acids Research 16(9):4077-4095 (1988) [Exhibit 45]
46. Agrawal, S. et al., "Efficient methods for attaching non-radioactive labels to the 5' ends of synthetic oligodeoxyribonucleotides," Nucleic Acids Research 14(15):6227-6245 (1986) [Exhibit 46]
47. Jablonski, E. et al., "Preparation of oligodeoxynucleotide-alkaline phosphatase conjugates and their use as hybridization probes," Nucleic Acids Research 14(15):6115-6128 (1986) [Exhibit 47]
48. Staerz, U.D. and Bevan, M.J., "Hybrid hybridoma producing a bispecific monoclonal antibody that can focus effector T-cell activity," Proc. Natl. Acad. Sci. USA 83:1453-1457 (1986) [Exhibit 48]
49. Fanger, M.W., "Bispecific Antibodies," Critical Reviews in Immunology 12(3,4):101-124 (1992) [Exhibit 49]

50. Gruber, M. et al., "Efficient Tumor Cell Lysis Mediated by a Bispecific Single Chain Antibody Expressed in *Escherichia coli*," Journal of Immunology 152:5368-5372 (1994) [Exhibit 50]
51. Holliger, P. et al., "'Diabodies': Small bivalent and bispecific antibody fragments," Proc. Natl. Acad. Sci. USA 90:6444-6448 (1993) [Exhibit 51]
52. Anderson, W.F. et al., "Structure of the cro repressor from bacteriophage and its interaction with DNA," Nature 290:754-758 (1981) [Exhibit 52]
53. Palsson, B.O. et al., "Expansion of Human Bone Marrow Progenitor Cells in a High Cell Density Continuous Perfusion System," Biotechnology 11:372368 (1993) [Exhibit 53]
54. Koller, M.R., et al., "Expansion of Primitive Human Hematopoietic Progenitors in a Perfusion Bioreactor System with IL-3, IL-6, and Stem Cell Factor," BioTechnology 11:358-363 (1993) [Exhibit 54]
55. Koller M.R. et al., "Large-Scale Expansion of Human Stem and Progenitor Cells From Bone Marrow Mononuclear Cells in Continuous Perfusion Cultures," Blood 82(2):378-384 (1993) [Exhibit 55]
56. Stavrianopoulos, J., U.S. Patent No. 4,843,122 issued June 27, 1989 [Exhibit 56]
57. Engelhardt, D. et al., European Patent No. EP 0 285 057 B1 granted March 1, 1995 [Exhibit 57]
58. Mount, S.M., "A catalogue of splice junction sequences," Nucleic Acids Research 10(2):472 (1982) [Exhibit 58]
59. Mayeda, A. and Oshima, Y., "Beta-globin transcripts carrying a single intron with three adjacent nucleotides of 5' exon are efficiently spliced in vitro irrespective of intron position or surrounding exon sequences," Nucleic Acids Research 18(16):4676 (1990)[Exhibit 59]
60. Chu, F.K. et al., "Intervening sequence in the thymidylate synthase gene of bacteriophage T4," Proc. Natl. Acad. Sci. USA 81:3049-3053 (1984) [Exhibit 609]

61. Chu F.K. et al., "In Vitro Expression of the Intron-containing Gene for T4 Phage Thymidylate Synthase," The Journal of Biological Chemistry 260(19):10680-10688 (1985) [Exhibit 61]
62. Muzyczka, N., "Use of Adeno-Associated Virus as a General Transduction Vector for Mammalian Cells," Current Topics in Microbiology and Immunology 158:97-129 (1992)] [Exhibit 62]
63. Rafestin, M.E. et al., "Purification of N-Acetyl D-Glucosamine-Binding Proteins By Affinity Chromatography," FEBS Letters 40(1):62-66 (1974) [Exhibit 63]
64. Lear, J.D. and DeGrado, W.F., "Membrane Binding and Conformational Properties of Peptides Representing the NH₂ Terminus of Influenza HA-2," The Journal of Biological Chemistry 262(14):6500-6505 (1987)] [Exhibit 64]
65. Kalderon D. et al., "A Short Amino Acid Sequence Able To Specify Nuclear Location," Cell 39:499-509 (1984) [Exhibit 65]
66. Stavrianopoulos J.G. et al., "Mechanism of DNA Replication by Highly Purified DNA Polymerase of Chicken Embryo," Proc. Nat. Acad. Sci. USA 69(9):2609-2613 (1972) [Exhibit 66]
67. Nitta, T. et al., "Bispecific F(ab')₂ monomer prepared with anti-CD3 and anti-tumor monoclonal antibodies is most potent in induction of cytolysis of human T cells," Eur J. Immunol. 19:1437-1441 (1989) [Exhibit 67]
68. Horton, R.M. et al., "Gene Splicing by Overlap Extension Tailor-Made Genes Using the Polymerase Chain Reaction," BioTechniques 8(5):528-535 (1990) [Exhibit 68]
69. Horton, R.M. et al., "Engineering hybrid genes without the use of restriction enzymes: gene splicing by overlap extension," Gene 77:61-68 (1989) [Exhibit 69]
70. Scharf, S.J. et al., "Direct Cloning and Sequence Analysis of Enzymatically Amplified Genomic Sequences," Science 233:1076-1078 (1986) [Exhibit 70]

71. Saiki, R.K., et al., "Enzymatic Amplification of Beta-Globin Genomic Sequences and Restriction Site Analysis for Diagnosis of Sickle Cell Anemia," Science 230:1350-1354 (1985) [Exhibit 71]
72. Kozak, M., "Point Mutations Define a Sequence Flanking the AUG Initiator Codon That Modulates Translation by Eukaryotic Ribosomes," Cell 44:283-292 (1984) [Exhibit 72]
73. Joshi, S. et al., "Inhibition of Human Immunodeficiency Virus Type 1 Multiplication by Antisense and Sense RNA Expression," Journal of Virology 65(10):5524-5530 (1991) [Exhibit 73]
74. Sczakiel, G. et al., "Specific inhibition of immunodeficiency virus type 1 replication by RNA transcribed in sense and antisense orientation from the 5'-leader/gag region," Biochemical and Biophysical Research Communication 169(2):643-651 (1990) [Exhibit 74]
75. Dunn, J.J. and Studier, F.W., "Complete Nucleotide Sequence of Bacteriophage T7 DNA and the Locations of T7 Genetic Elements," J. Mol. Biol. 166:477-535 (1983) [Exhibit 75]
76. Sandig V. et al., "A phage λ class-III promoter functions as a polymerase II promoter in mammalian cells," Gene 131:255-259 (1993) [Exhibit 76]
77. Harrison G.S. et al., "Inhibition of Human Immunodeficiency Virus-1 Production Resulting from Transduction with a Retrovirus Containing an HIV-Regulated Diphtheria Toxin A Chain Gene," Human Gene Therapy 3:461-469 (1992) [Exhibit 77]
78. Manser, T. and Gesteland, R.F., "Human U1 Loci" Genes for Human U1 RNA Have Dramatically Similar Genomic Environments," Cell 29:257-264 (1982) [Exhibit 78]
79. McBurney M.W. et al., "The mouse Pgk-1 gene promoter contains an upstream activator sequence," Nucleic Acids Research 19(20):5755-5761 (1991) [Exhibit 79]
80. Laurence, J. et al., "Induction of Chronic Human Immunodeficiency Virus Infection Is Blocked In Vitro by a Methylphosphonate Oligodeoxynucleoside

Targeted to a U3 Enhancer Element," The Journal of Virology 65(1):213-219 (1991) [Exhibit 80]

81. Soeiro, R. and Darnell, J.E., "Competition Hybridization by "Pre-saturation" of HeLa Cell DNA," J. Mol Biol 44:551-562 (1969) [Exhibit 81]

The above eighty-one documents [Exhibits 1-81] were cited in the instant specification.

A completed Form PTO-1449 listing the eighty-one above-submitted documents is also attached hereto as Exhibit A.

By this voluntary citation of art, Applicants and their attorney are requesting that the documents be made of record in the present application.

The above citation of documents is not a representation that these documents constitute a complete or exhaustive listing, nor that the above listing necessarily includes the closest or most relevant documents, nor are these documents necessarily a complete listing of all documents known to Applicants or their attorney. It is simply a voluntary citation of documents made in good faith, which is not intended to serve in any way as a substitute for the Examiner's own search.

In view of the general and specific features described and claimed in the present application, Applicants respectfully submit that the present invention is neither disclosed nor suggested by the documents referred to above and is thus patentably distinct thereover. Furthermore, Applicants do not believe, and do not submit, by the citation of these references, that these documents, either by themselves or in combination with other documents, render the invention *prima facie* obvious under the duty of disclosure rules.

Applicants respectfully request that the Examiner make the above-submitted documents of record in the instant application. Applicants further request that the

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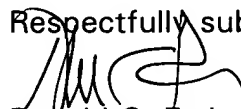
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Examiner consider these documents as any of them may relate to the instant application.

The fee under 37 C.F.R. §1.17(p) for filing this Information Disclosure Statement is \$180.00. The Patent and Trademark Office is hereby authorized to charge the amount of this fee (and any other fees in connection with this IDS) to Deposit Account No. 05-1135, or to credit any overpayment thereto.

Respectfully submitted,



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* No document or publication is being submitted for this Exhibit due to technical difficulties.